

CLAIMS

1. Markers of the neurodegenerative process, constituted by the ATP synthase α chain having undergone pathological modifications resulting from said process.
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2. Markers according to claim 1, characterized in that the modifications of the ATP synthase α chain are of functional, location, structural and/or antigenic type.
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3. Markers according to any one of the preceding claims, characterized in that the neurodegenerative process is that of any pathology with a neurofibrillary degeneration process and aggregation of tau proteins, in particular, that of
15 Alzheimer's disease.
4. Markers according to claim 3, characterized in that one of the functional modifications of the ATP synthase α chain is its insolubility.
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5. Markers according to claim 3 and/or 4, characterized in that one of the location modifications of the ATP synthase α chain is its location in the cytoplasm of the cell.
- 25 6. Markers according to claim 3, characterized in that one of the structural modifications of the ATP synthase α chain is the formation of aggregates at the level of the cerebrum.
7. Markers according to any one of the preceding claims,
30 characterized in that they interact with the tau proteins.

8. Method of detection and/or of diagnosis in vitro of the neurodegenerative process, characterized in that one of the markers according to one of claims 1 to 7 is detected in a sample to be analyzed.

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9. Method according to claim 8, characterized in that it comprises the use of sets of antibodies directed against the normal protein and/or against modifications of the ATP synthase α chain.

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10. Method according to any one of claims 8 or 9, characterized in that it is used for detection of the degenerative process of any pathology with a neurofibrillary degeneration process and aggregation of tau proteins, in particular that of Alzheimer's disease.

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11. Method according to any one of claims 8 to 10, characterized in that immuno-chemical detection is used, in particular by 1D and/or 2D electrophoresis coupled with an immunodot, development by polyclonal antibodies or monoclonal antibodies directed against the ATP synthase α chain, immuno-assay and/or radioimmuno-assay, optionally completed by mass spectrometry analysis.

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12. Method according to any one of claims 8 to 11, characterized in that the samples to be analyzed used in said method include neuronal tissues or cells, non-neuronal tissues or cells, in particular biological liquids, preferably blood.

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13. Diagnostic method according to any one of claims 8 to 12, characterized in that the degree of pathology is

moreover evaluated by establishing an index based on the relationship between the normal level of the ATP synthase α chains in control subjects in a defined protein fraction, with respect to the level observed at an advanced stage of
5 Alzheimer's disease.

14. Diagnostic method according to any one of claims 8 to 13, characterized in that the degree of pathology is moreover evaluated by establishing an index based on
10 modifications of the ATP synthase α chain in a patient compared with a control subject.

15. Uses of the method according to claims 8 to 14, for assisting with ante and post-mortem diagnosis of the neurodegenerative diseases, in particular Alzheimer's
15 disease, at the subclinical stage.

16. Animal or cell model, characterized in that it expresses an ATP synthase α chain having a maturation signal defect or a post-translational modification anomaly.
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17. Use of the method according to any one of claims 8 to 14 or of the model according to claim 16, for pharmacological screening and therapeutic tests on molecules
25 effective against the neurodegenerative pathologies, in particular of Alzheimer's disease type.

18. Use of the method according to any one of claims 8 to 14, in order to establish and validate cell models and/or
30 animal models of neurodegenerative pathologies, in particular of Alzheimer's disease.

19. Use of a kit for the detection of the ATP synthase α chain, for the diagnosis of neurodegenerative diseases, in particular for the detection of Alzheimer's disease.

5 20. Polyclonal and/or monoclonal antibodies directed against patterns of pathological conformation of the ATP synthase α chain resulting from a neurodegenerative process.

21. Diagnostic kit characterized in that it comprises sets
10 of antibodies according to claim 20.

22. Diagnostic kit according to claim 21, characterized in that said kit contains reagents making it possible to carry out an immunochemical assay, in particular of ELISA,
15 immunodot, Western blots, dots-blots, radioimmuno-assay or immuno-assay type.